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Case Series

Pathology Section

Extra-lymphatic Filariasis: A Study of Three Interesting Cases

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ABSTRACT

Filariasis is a chronic disabling parasitic disease that causes a major public health problem in tropical countries like India. *Wuchereria bancrofti* is associated with almost 99.4% of cases. Filariasis not only affects the structure and function of lymphatic vessels but is also associated with extra-lymphatic pathology and diseases. Lymphatic filariasis is commonly found throughout the tropics and subtropics. While lymph nodes are the common sites, unusual sites include the breast, spleen, subcutaneous tissue, thyroid, bone marrow, urinary tract, sputum, bronchial washing, pleural and pericardial fluid. Patients from endemic areas presenting with swelling should be evaluated for filariasis. Here in present case series, the authors discussed three cases: filariasis of the breast with fibroadenoma, soft-tissue nodule, and splenic lesions, due to their extreme rarity and unusual sites. In the first case, 20 years old female patient presented with a lump in the left breast. The Complete Blood Cell (CBC) revealed eosinophilia, but peripheral smears did not show the presence of microfilariae. On Fine Needle Aspiration Cytology (FNAC), smears showed *Wuchereria bancrofti* microfilaria in the background of fibroadenoma. The patient was treated with Diethylcarbamazine (DEC) for 21 days. Repeat CBC revealed a decrease in the absolute eosinophil count. Lumpectomy for fibroadenoma was performed, which showed fragments (dead) of the microfilarial parasite. The association of filariasis with fibroadenoma is possibly due to pre-existing subclinical filariasis when the neoplasm developed, as the patient hails from an endemic area. Filariasis presenting as a soft-tissue nodule is an uncommon incidence. In the second case discussed here, 30 years old female patient had soft-tissue swelling over the left elbow. Peripheral smear only revealed eosinophilia without any parasites. On FNAC, smears showed *Wuchereria bancrofti* microfilaria, along with lymphoid cells and a few eosinophils. The swelling subsided with DEC treatment, and repeat CBC showed a decrease in the absolute eosinophil count. The third case discussed here, involved an unknown 35 years old male, who was brought dead to the hospital. No clinical details were available. On autopsy, the spleen showed multiple white patches, ranging in size from 0.2 to 0.5 cm in diameter. All other organs were unremarkable. Microscopy showed many granulomas and numerous dead fragmented microfilariae. It was a case of isolated splenic filariasis, which is a rarely diagnosed entity. These unique cases will raise awareness of diagnosing and instituting proper therapy.

Keywords: Breast, Disabling, Parasitic disease, Soft-tissue, Spleen

INTRODUCTION

Filariasis is a chronic disease of the lymphatic and extra-lymphatic systems, creating significant social and health issues in tropical nations like India. It is most commonly caused by *Wuchereria bancrofti*.

In the case of filariasis, man is the primary host, while the mosquito serves as the secondary host [1]. In India, lymphatic filariasis is caused by the nematode worms *Wuchereria bancrofti, Brugia malayi, and Brugia timori*, with *Wuchereria bancrofti* responsible for nearly 99.4% of cases and B. malayi for 0.6% [2]. In India, 250 districts in 20 states are endemic for filariasis [3].

Filariasis is transmitted by the Culex mosquito, and its lifecycle is divided into mosquito and human phases. The definitive host is man, and the intermediate host is the mosquito. The mosquito phase begins when microfilariae are picked up by the vector mosquito during its blood meal. Four stages of development can be observed: a) ex-sheathing of the larva; b) first-stage larva; c) second-stage larva; and d) third-stage larva (infective form) [4]. The infective form, microfilaria, does not trigger a significant inflammatory response. After the death of the adult worm residing in the lymphatics and lymph nodes, a granulomatous reaction occurs [5]. The usual diagnosis of filariasis relies on screening peripheral blood smears for microfilariae. However, incidental microfilariae can be observed in various cytological specimens [6]. There are occasional reports of extra-lymphatic microfilariae in other locations such as the breast, skin, soft-tissue swellings, and thyroid [6]. The authors hereby report three cases of microfilariae in rare extra-lymphatic sites, like breast, soft tissue, and spleen.

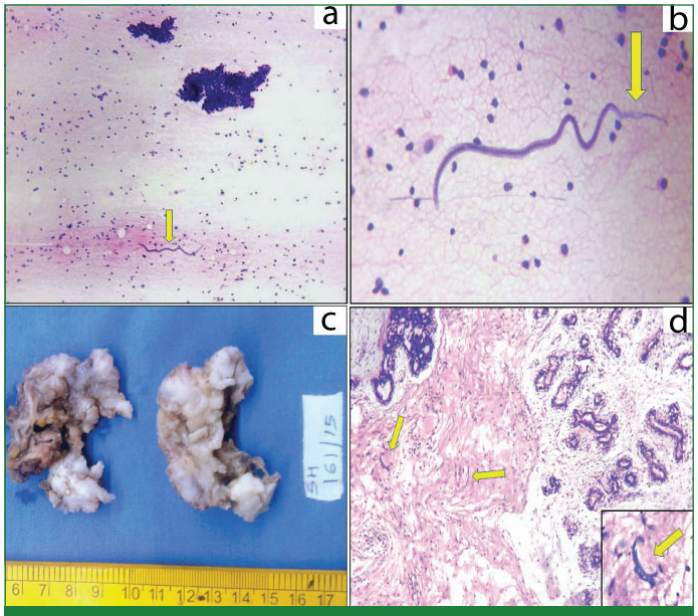
CASE SERIES

Case 1

A 20-year-old female patient presented with a gradually increasing lump in the left breast since eight months. During the history-taking, it was revealed that the patient had a history of moderate-grade fever without chills since two months. On clinical examination, a well-defined, non-tender, freely mobile lump measuring 2.5×2.5 cm was palpable in the upper and outer quadrant of the breast. There was no evidence of lymphadenopathy or hepatosplenomegaly. The CBC revealed mild eosinophilia with an absolute eosinophil count of 720/cmm (0 to 500 /cmm). Peripheral smears did not show the presence of microfilariae. Investigation of FNAC of the breast lump showed monolayered sheets and clusters of benign ductal epithelial cells, suggesting a fibroadenoma [Table/Fig-1a]. The smears also showed a few sheathed microfilariae with nuclei-free tail tips [Table/Fig-1b].

A diagnosis of fibroadenoma with filarial infestation by *Wuchereria bancrofti* was made. The patient was treated with DEC (dosage: 6mg/kg) for 21 days. Repeat CBC revealed a decrease in the absolute eosinophil count to 170/cmm. Subsequently, the patient underwent lumpectomy. Grossly, the lump had a grey-white myxoid

appearance on the cut surface with slit-like spaces [Table/Fig-1c]. Histopathology showed features of fibroadenoma with the presence of fragments of microfilarial parasites in the interlobular stroma, confirming the diagnosis of fibroadenoma with the presence of microfilarial parasites [Table/Fig-1d]. Sparse lymphocytic infiltrate with occasional eosinophils was observed. However, a granulomatous reaction was not seen. Hence, the diagnosis of Bancroftian filariasis of the breast with fibroadenoma was established. After the lumpectomy, the symptoms resolved.

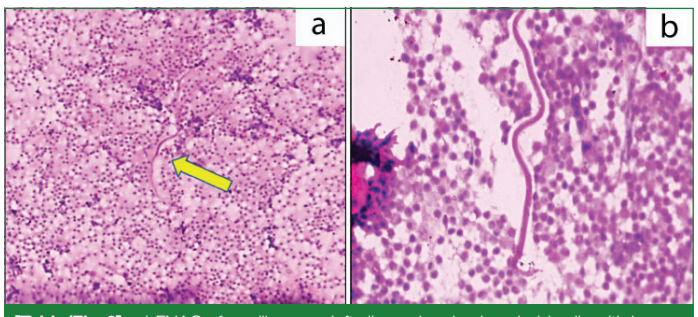


[Table/Fig-1]: a) FNAC breast showing monolayered sheets and clusters of benign ductal epithelial cells with filarial parasite (↑) (H&E, 40X); b) FNAC breast showing sheathed microfilariae (*Wuchereria bancrofti*), with tail tip free from nuclei (↑) (H&E, 100X); c) Gross specimen of lumpectomy -Fibroadenoma; d) Histopathology section of lumpectomy showing fibroadenoma and presence of microfilarial parasite (↑) (H&E, 40X) with inset showing high power image of microfilaria (↑) (H&E, 100X).

Case 2

A 30-year-old female patient presented with swelling in the left elbow for the past two years. The swelling was not associated with pain, tingling, or numbness. There was no history of trauma, fever, cough, cold, weight loss, or loss of appetite. The patient had no past history of tuberculosis or contact with tuberculosis. There were no known medical conditions such as hypertension, diabetes, or bronchial asthma.

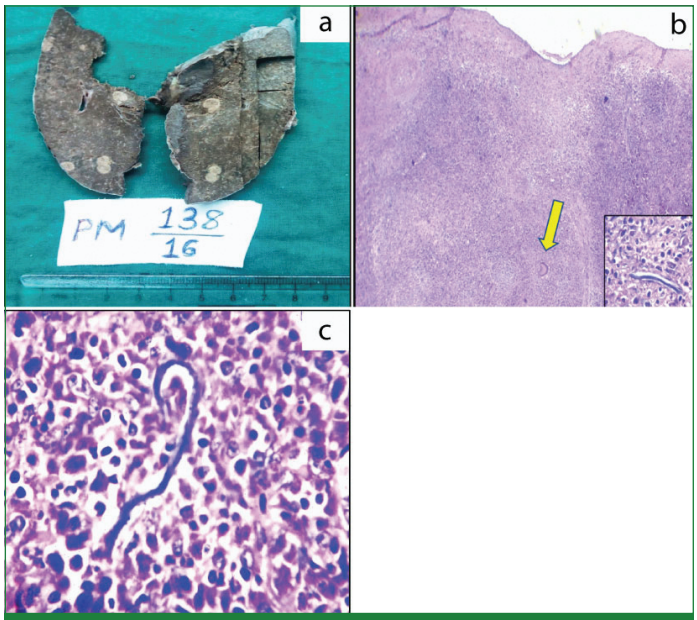
CBC revealed mild eosinophilia (absolute count 600/cmm), and no parasites were seen on peripheral smear. Ultrasound showed a hypoechoic lesion in the anterolateral aspect of the left elbow. The differential diagnosis based on ultrasound was a nerve sheath tumour. On investigation, FNAC of the swelling revealed a polymorphic population of lymphoid cells mixed with a few eosinophils. Additionally, occasional sheathed microfilaria larvae with nuclei-free tail tips were observed, along with epithelioid granulomas. There was no evidence of caseation necrosis. The diagnosis of a granulomatous lesion with microfilaria infestation (*Wuchereria bancrofti*) was made [Table/Fig-2]. The patient was treated with DEC (dosage: 6 mg/kg) for 21 days, and the swelling subsided. Repeat CBC showed an absolute eosinophil count of 200/cumm.



[Table/Fig-2]: a) FNAC of swelling over left elbow showing lymphoid cells with larvae of microfilaria (↑) (H&E 10X); b) FNAC of swelling over left elbow showed sheathed microfilariae with nuclei free tail tip (H&E 100X).

Case 3

A 35-year-old unknown male was brought dead to the hospital, and an autopsy was performed. The spleen showed multiple, white patches ranging in size from 0.2 to 0.5 cm in diameter [Table/Fig-3a]. On autopsy, all other organs appeared unremarkable grossly. Microscopic examination revealed numerous granulomas [Table/Fig-3b] and fragmented microfilariae in a deceased state [Table/Fig-3c]. Since the patient's identity was unknown and there were no available clinical details, only the spleen exhibited the mentioned histopathological findings. The other organs were unremarkable both grossly and microscopically. Therefore, the authors consider splenic filariasis to be an incidental finding encountered during post-mortem histopathological examination.



[Table/Fig-3]: a) Gross specimen of spleen-multiple, white patches of size ranging from 0.2 to 0.5 cm in diameter; b) Microscopy showing splenic parenchyma with granulomatous inflammation (↑) (H&E 10X). Inset shows sheathed microfilariae (H&E 40X); c) Microscopy showing microfilaria (H&E 100X).

DISCUSSION

According to the World Health Organisation (WHO), Filariasis is identified as a significant global health problem that causes permanent and long-term disability [7]. Lymphatic filariasis is found in heavily infected states such as Uttar Pradesh, Bihar, Jharkhand, Andhra Pradesh, Orissa, Tamil Nadu, Kerala, and Gujarat. In India, *Wuchereria bancrofti* and *Brugia malayi* are mainly responsible for filariasis. Morphologically, both have sheathed microfilariae. The tail tip of *Wuchereria bancrofti* is free of nuclei, while that of *Brugia malayi* shows terminal two nuclei. In endemic countries, *Wuchereria bancrofti* is responsible for 98% of infections [7].

The microfilariae are released into the peripheral circulation, while the adult worm resides in the lymphatics of the hosts [6]. Extravasation of the larval form occurs due to lympho-vascular obstruction, potentially reaching the tissue space [8]. The lymphatics of the spermatic cord, epididymis, mammary glands, lower limbs, and retroperitoneal tissue are most frequently affected [6]. In this case series, first two cases did not show microfilariae on peripheral smear but showed filariasis on FNAC of the breast and soft tissue. Thus, filariasis can exist without microfilaremia, as reported by many authors [4,9]. Both cases showed eosinophilia on CBC. Yenkeshwar PN et al., in their report of 22 cases of microfilariae in FNA from various sites, similarly found eosinophilia in five cases [6].

Filariasis should be considered as a differential diagnosis in patients presenting with subcutaneous nodules in filarial endemic zones, as

seen in the present two FNAC cases who hailed from Uttar Pradesh. Eosinophilia on peripheral smear and cytology provide supporting findings for the diagnosis of filariasis. The morphology of microfilariae on FNAC smears helps identify the species. In these cases, both were morphologically *Wuchereria bancrofti*. FNAC diagnosis of microfilariae is important for early diagnosis and medical treatment, which avoids further surgical intervention [6].

In breast filariasis, lymphangitis and fibrosis are caused by lymphatic obstruction. It may mimic malignancy, as it can present with enlargement of axillary nodes and hyperemia of the overlying skin, resulting in a peau d'orange appearance [4,10,11]. Rarely, microfilariae coexist with neoplastic lesions. Yenkeshwar PN et al., found microfilariae in three cases of the breast, one of which was associated with infiltrating duct carcinoma [6]. Pantola C et al., in their series of seven cases, reported microfilariae coexisting with six malignant lesions, including one case of breast adenocarcinoma, and one benign lesion, pleomorphic adenoma of the parotid gland [12]. Gupta N and Chawla A reported a case of filariasis of the breast, clinically masquerading as fibroadenoma [11]. Filariasis against background of fibroadenoma is an extremely rare association, which was observed in one of the presently discussed cases. The association of filariasis with fibroadenoma is possibly because of pre-existing subclinical filariasis, as the patient hails from an endemic area (UP) [4]. Some authors have suggested increased vascularity associated with lesions as a cause for the presence of microfilaria in neoplasms [12]. The present findings correlate with similar reported literature [Table/Fig-4a].

Skin and soft-tissue swelling, breast, thyroid, salivary glands, cervicovaginal smears, ovarian cysts, effusion fluids, urine, bronchial, laryngeal, and pharyngeal brushings are infrequent sites where extranodal filariasis has been documented [6]. In studies conducted by Yenkeshwar PN et al., and Mishra R et al., soft tissue and breast were common sites [6,13]. People in endemic areas get infected early in life and develop microfilaremia between 15-20 years of age [13]. Several studies of subcutaneous swelling showing microfilaria have been tabulated, which correlate with the present findings [Table/Fig-4b].

In the third case, autopsy showed isolated splenic filariasis with multiple non-necrotising granulomatous lesions on histopathology. Although filariasis is ubiquitous and frequently present in India, it rarely results in splenic symptoms as observed in here. Dhayagude RG and Amin BM documented that filariasis can produce lesions in the spleen with or without eosinophilia and concluded that it can be an incidental finding [14]. Hence, in cases of multiple splenic granulomatous lesions, the differential diagnosis of splenic filariasis should be considered [Table/Fig-4c] [1,3,14-22].

a. Author	Place of case reported	Year	FNAC findings	Species
Current study	Maharashtra, India	2023	Fibroadenoma with sheathed microfilariae with nuclei free tail tips.	*Wuchereria bancrofti*
Priyadharisini J et al., [15]	Puducherry, India	2022	Neutrophils, foamy histiocytes, granulomas and many microfilariae.	*Wuchereria bancrofti*
Nanda A and Shastri M [16]	New Delhi, India	2022	Case-1: Microfilaria with mixed inflammatory cells in the background.	*Wuchereria bancrofti*
			Case-2: Microfilaria with mixed inflammatory infiltrate and macrophages.	*Wuchereria bancrofti*
Trivedi P [17]	Barabanki, Uttar Pradesh, India	2021	Microfilaria with background of mature lymphocytes.	*Wuchereria bancrofti*
Vyas S et al., [3]	New Delhi, India	2020	Microfilariae in the background of lymphocytes.	*Wuchereria bancrofti*
Barwad A et al., [18]	New Delhi, India	2018	Microfilaria, adult and embryonated eggs of adult gravid female worm.	*Wuchereria bancrofti*

b. Author	Place of case reported	Year	FNAC findings	Species
Current case	Maharashtra, India	2023	Lymphoid cells with few eosinophils with larvae of microfilaria with epithelioid granulomas.	*Wuchereria bancrofti*
Chatterjee R et al., [19]	Kolkata, India	2021	Microfilaria along with blood components.	*Wuchereria bancrofti*
Sahoo N et al., [20]	Bhubaneswar, Odisha, India	2019	Few lymphocytes, cyst macrophages, neutrophils, and histiocytes over a fluid-like background.	*Wuchereria bancrofti*
Nanda A et al., [21]	New Delhi, India	2018	Adult gravid female filarial worm and different stages of developing microfilaria.	*Wuchereria bancrofti*
Adhikari P et al., [1]	Dharan, Nepal	2018	Microfilariae with a clear space of nuclei at its caudal end.	*Wuchereria bancrofti*

c. Author	Place of case reported	Year	Postmortem findings-microscopy	Species
Current study	Maharashtra, India	2023	Many granulomas and numerous dead fragmented microfilariae.	*Wuchereria bancrofti*
Nigudgi S et al., [22]	Kalaburagi, Karnataka, India	2018	Splenic nodules with eosinophils, macrophages and foreign body giant cells. Macrophages surrounded by filariasis parasite.	Not specified

[Table/Fig-4a-c]: Comparison of the current study with similar reported literature in last 5 years [1,3,15-22]. a: Breast filariasis; b: Subcutaneous swelling; c: Splenic filariasis.

The diagnosis of filariasis is made by demonstrating microfilaria in stained or unstained blood films and detecting filarial antigen at low levels of microfilaremia. The majority of affected individuals remain asymptomatic, with continued disease transmission in endemic areas [5].

CONCLUSION(S)

In a patient coming from endemic areas of filariasis with a lump at any site, one should keep the possibility of filariasis in mind. Careful screening of cytology slides for microfilariae should be done. Fine-needle Aspiration Cytology (FNAC) of these nodules can be really helpful in such cases, and an awareness and active search for an adult worm or microfilaria should be undertaken for an accurate diagnosis. When considering a case of multiple symptomatic/asymptomatic splenic granulomatous lesions, the differential diagnosis of splenic filariasis should be taken into account.

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